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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/750,846	01/05/2004	Heimo Haikala	06267.0116	3865

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/750,846	HAIKALA ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 3 AND 5 ARE PRESENTED FOR EXAMINATION

Applicants' amendment filed March 21, 2007 has been received and entered into the application. Accordingly, claims 3 and 5 have been amended. In light of the amendments, the rejection of claims 3 and 5 under 35 U.S.C. § 112, first paragraph, as set forth in the previous Office action dated September 27, 2006, has been overcome and thus is here *withdrawn*.

Also, because it appears that administration of levosimendan is necessary for conversion, *in vivo*, to dextrosimendan, i.e. the R-enantiomer as claimed, Verheugt would not teach a pharmaceutical composition comprising the claimed compound. Accordingly, the rejection of claims 3 and 5 under 35 U.S.C. § 102(b) has been overcome and is here *withdrawn*.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejection - 35 USC § 103

Claims 3 and 5 remain rejected under 35 U.S.C. 103(a) as being obvious over Haikala et al. (U.S. RE38,102, "Haikala '102"), Haikala et al. (U.S. Patent No. 5,905,078; "Haikala et al. '078") or Applicants' acknowledgment at page 1, lines 2-4 of the third paragraph, **or** Sircar (U.S. Patent No. 4,397,854) in view of Campbell (U.S. Patent No. 4,432,979) and Diamond et al. (U.S. Patent No. 4,517,310), in further view of Verheugt. each of record, for the reasons of record as set forth in the previous Office action at pages 9-10, which reasons are here incorporated by reference and in further view of Applicants' acknowledgment at page 1 of the present specification, third paragraph, "The compound (I) has an asymmetric...".

Applicants' remarks and the amendments to the claims, as noted above, have been carefully considered, but fail to persuade the Examiner of error in his determination of obviousness.

In traversing the continued rejection of the claims, Applicants have remarked that Verheugt does not disclose a pharmaceutical composition comprising the R-enantiomer of N-[4-(1,4,5,6-tetrahydro-4-methyl-6-oxo-3-pyridazinyl)phenyl]acetamide (I). This does not diminish the propriety of the present rejection, however, because Verheugt was not relied on for this teaching. Rather, it was relied on to buttress the Examiner's conclusion that the activity of the claimed compound in heart failure patients would not have been expected to be detrimental to mortality.

Applicants' further remark that the data in Verheugt is insufficiently detailed to assess the activity of the R-enantiomer of compound (I). In response, the Examiner believes that the activity of levosimendan in Verheugt would have at least suggested to one of ordinary skill the activity for the R-enantiomer of compound (I) given its close structural similarity.

Also, from the above, Applicants' conclude that the Examiner has failed to show that any of the cited references, alone or in combination, suggest any mortality reducing effect of the R-enantiomer of compound (I) in patients suffering from congestive heart failure. The Examiner cannot agree, however, given the teachings in the primary references already relied on. In particular, that the R-enantiomer of compound (I) was effective against congestive heart failure. It would not follow then that this compound would have been expected to increase mortality in patients suffering from congestive heart failure.

Applicants have taken issue with the above by pointing out that positive inotropic agents have been associated with an increase in mortality. Applicants have contended that the presently claimed compound was also a positive inotrope and thus would not have been expected to increase mortality. In support of this position, Applicants have pointed to Kasper, (cited in the previously filed form PTO-1449), where it was allegedly taught that positive inotropic agents, which Applicants contend that the claimed compound was a member, "produce striking short-term benefits but increase mortality in patients with left ventricular dysfunction", (see Applicants' response dated May 30, 2006 at page 5).

The Examiner cannot agree with Applicants' position. Initially, it is noted that the claims do not specify left ventricular dysfunction. The Examiner cannot agree further because it has not been established that the presently claimed compound would have been viewed in the same light as the other inotropic agents. The Examiner notes in Haikala et al., (U.S. Patent No. 5,905,078), that the R-enantiomer is apparently distinguished over other inotropic agents such that it would not have been expected that the R-enantiomer would cause arrhythmias such as with other inotropic agents. In particular, Haikala et al. at col. 1, lines 22-64 indicates that the R-enantiomer of compound 1 has a calcium sensitizing effect on troponin and that is its main mechanism to increase cardiac contractility, (lines 55+). This is beneficial as compared to other inotropic agents which in contrast "increase the contractility of the cardiac muscle by increasing the calcium current into the cardiac muscle and cause vasodilation. The contraction in cardiac muscle is triggered by the binding of calcium in troponin. However, it is possible that long-term application of [other inotropic agents] leads to calcium overload in the cardiac muscle which can trigger arrhythmias", (lines 22+).

Accordingly, it is still maintained that the claimed subject matter is not patentable over the cited references.

None of the claims are currently in condition for allowance.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Raymond J Henley III
Primary Examiner
Art Unit 1614

June 8, 2007